REMARKS

Claims 1-20, 39, and 41-75 are canceled. Claims 21-38, 40, and 76-93 are pending and under consideration. The pending claims are currently rejected under 35 U.S.C. 103(a). No amendments are made in this paper.

In response to the instructions in the Office Action to insert the application serial number on all pages of amendments, Applicants confirm that the serial number appears on every page of this paper. However, the serial number of this application does not appear on the attachments to this paper because the attachments are copies of laboratory pages that we have only altered with respect to redaction of the date.

TELEPHONE INTERVIEW SUMMARY

Applicants thank the Examiner for the courtesy of a telephone interview on January 31, 2007. Participants were Examiner Irene Marx, and Applicants' representatives Margaret Brivanlou and Michael Willis. The substance of the interview was a discussion of the procedural requirements for the papers filed on September 27, 2006. In particular, Applicants requested guidance from the Examiner on overcoming the Examiner's objections to certain exhibits to the 131 Declaration filed with the September 27, 2006 Amendment. The Examiner indicated that clearer and complete copies of the pages of the exhibits to which she had objected should be sufficient but that any decisions or suggestions would only be made in the context of an official Office Action in response to formal submissions.

REJECTION UNDER 35 U.S.C. § 103(a)

Summary of rejection

Claims 21-38, 40 and 75-93 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Davenport *et al.* (Pediatric Pulmonology, S13 Abstract 34, August 16, 1996) taken with Ubillas *et al.*, Masquelier, Wursch and Remington's Pharmaceutical Sciences and Applicants' admissions. Applicants respectfully traverse the rejection. In addition, Applicants note that claim 75 was previously canceled and is not pending.

The cited references do not render the claimed invention obvious

Applicants have previously provided arguments with respect to the combined references. Applicants refer to the arguments in the papers submitted September 27, 2006. There is no suggestion, much less any teaching, in Davenport for the isolated proanthocyanidin polymer from Croton to be enterically protected in order to be useful for use as an anti-diarrheal agent. Davenport's disclosure of administering proanthocyanidin in $NaHCO_3$, relative to $NaHCO_3$ alone, to inhibit fluid accumulation in the cholera toxin-induced model of secretory diarrhea, does not render the herein claimed subject matter obvious. Davenport does not suggest to a person of ordinary skill that the isolated proanthocyanidin polymer composition must be formulated to protect the proanthocyanidin polymer composition from the stomach environment. While Davenport happened to use the buffer $NaHCO_3$ to formulate the SP-303 for administration by gavage, Davenport does not teach or suggest what the inventors of the instant application have discovered, *viz.*, to be effective for treatment of diarrhea, the proanthocyanidin formulation must somehow be protected from the acid environment of the stomach. Thus, Davenport does not suggest formulating the claimed proanthocyanidin polymer composition to protect it from the stomach environment as a controlled release preparation or to coat the composition with an

enteric coating and, thus, does not render the invention obvious. Applicants refer to the previous discussion of the remaining references on pages 11-12 of the September 27, 2006 submission.

In addition, the Examiner has indicated that

"With respect to the assignment issue and 103(c), it is noted that MPEP 706.02(1)(2) states that:

> The statement concerning common ownership should be clear and conspicuous (e.g., on a separate piece of paper or in a separately labeled section) in order to ensure that the examiner quickly notices the statement. Applicants may, but are not required to, submit further evidence, such as assignment records, affidavits or declarations by the common owner, or court decisions, in addition to the above-mentioned statement concerning common ownership.

Applicant has failed to follow these guidelines."

Accordingly, Applicants reiterate the statement regarding common ownership on the page that follows on a separately labeled page so as to comply with the Examiner's request.

The remainder of this page is left blank.

Davenport reference is not evidence of prior art under 35 U.S.C. § 102(f) or (g)

Applicants wish to inform the Examiner that Shaman Pharmaceuticals, Inc. and the University of North Carolina are parties to a joint research agreement.

Section (c)(2) of 35 U.S.C. § 103 states the conditions under which subject matter developed by another person and a claimed invention shall be deemed to have been owned by the same person or subject to an obligation of assignment to the same person. In accordance with Section (c)(2) of 35 U.S.C. § 103, Applicants submit that (A) the invention disclosed and claimed in the present application was made by or on behalf of Shaman Pharmaceuticals, Inc. and the University of North Carolina as parties to a joint research agreement that was in effect prior to the date the claimed invention was made; (B) the claimed invention was made as a result of activities undertaken within the scope of the research agreement; and (C) the application has been amended in the paper submitted September 27, 2006 to disclose the names of the parties to the joint research agreement.

Therefore, under Section (c)(2) of 35 U.S.C. § 103, the Davenport reference and the work reported therein is not evidence of prior art under 35 U.S.C. § 102(f) or (g). As such, Davenport and the work reported therein are not available for a rejection under 35 U.S.C. 103(a).

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Davenport reference is not prior art under 35 U.S.C. § 102(a)

> The Office Action states that
>
> Applicant's arguments and declarations have been fully considered but they are not deemed to be persuasive.
> Applicant's declarations attempting to antedate the Davenport reference are defective in that the report # SP-303-E-074 is not executed. In addition, the signatures on Notebook 368 are absent or cut-off.

(See Office Action, page 4 under heading "Response to Arguments").

As there are no comments as to the substance of the Declaration of the Inventors under 37 CFR 1.131 ("131 Declaration") submitted on September 27, 2006, and the "arguments and declarations have been fully considered", Applicants understand the Examiner's comments to mean that addressing the Examiner's concerns as to the format of the 131 Declaration exhibits will successfully antedate the Davenport reference and overcome the Examiner's rejection.

Applicants hereby submit re-scanned copies of Exhibit 4. The original Exhibit 4 as attached to the 131 Declaration contained scans of the laboratory notebook cover, page 54 (top half), page 54 (bottom half), and pages 55-57. The signatures on pages 54 (bottom half) and 56-57 were inadvertently omitted during the original scanning process. The attached re-scanned copies of Exhibit 4 include higher resolution scans of the laboratory notebook cover, page 54 (as a single page), and pages 55-57. The signatures on pages 54 and 56-57 are now legible. The attached re-scanned copies of Exhibit 4 are the same documents as submitted on September 27, 2006, only re-scanned from the original for clearer reproduction. Dates have been redacted according to standard practice for submission of exhibits to declarations. In addition, Applicants include cropped and enlarged portions of Exhibit 4, corresponding to the tables on pages 54-56 and the graph on page 57 for the convenience of the Examiner.

Applicants do not have a version of the report # SP-303-E-074, which was attached as Exhibit 2 to the 131 Declaration, that has been executed by Dr. Sabouni and Ms. King. Applicants submit that an executed version is unnecessary in view of the statements in the 131 Declaration that Dr. Sabouni and Ms. King were authors of the document, that it describes experiments carried out by one or more of the inventors, or by others under their direction, and that it is dated prior to August 16, 1996. However, should the Examiner disagree, Applicants submit that the 131 Declaration and the signed notebook pages of Exhibits 3 and 4 should provide ample evidence that the inventors had conceived of and reduced to practice the claimed invention prior to August 16, 1996.

Applicants specifically direct the Examiner's attention to Exhibit 4, page 56, which includes a bar graph entitled "Experiment 8: Effect of Enteric Coated SP-303 on Fluid Accumulation in Cholera Toxin-Treated Mice." This laboratory page by itself and in combination with the 131 Declaration and the other exhibits proves that the presently claimed invention was conceived and reduced to practice prior to the August 16, 1996 publication date of Davenport. The chart in Experiment 8 shows that cholera-treated (CT) mice when treated with 131 mg/kg enteric coated SP-303 showed 0.71 mg fluid / mg intestine as compared with 1.28 or 1.15 mg fluid / mg intestine for the control animals. Thus, this chart documents that the inventors, prior to the August 16, 1996 publication date of Davenport, had shown that an enteric coated proanthocyanidin polymer composition from *Croton lechleri* was effective to reduce fluid accumulation in mouse models of secretory diarrhea, a reduction to practice of the instantly claimed invention. Applicants respectfully request that any response by the Examiner specifically address the substance of the Declaration in relation to the notebook pages with charts entitled "Experiment 7: Effect of Enteric Coated SP-303 on Fluid Accumulation in Cholera

Toxin-Treated Mice" and "Experiment 8. Effect of Enteric Coated SP-303 on Fluid Accumulation in Cholera Toxin-Treated Mice".

As set forth in the response filed September 27, 2006, since the Rule 131 Declaration has demonstrated that the inventors conceived of and that the inventors or persons acting under the direction of the inventors reduced to practice the claimed methods of treating secretory diarrhea prior to August 16, 1996, Davenport is not available as prior art against the claimed methods under 35 U.S.C. § 102(a). As Davenport is not available to combine with other references under 35 U.S.C. § 103(a), Applicants respectfully request withdrawal of the rejection.

Without Davenport, the remaining references do not render the claimed invention obvious

As discussed above and in previous submissions, Applicants traverse the rejection over the combination of cited references. Davenport is not available as prior art, as discussed above. The remaining references fail to render the claimed invention obvious. The combination of the remaining references (Ubillas *et al.*, Masquelier, Wursch and Remington's Pharmaceutical Sciences and Applicants' admissions) has been discussed in detail in the previous responses. Applicants specifically refer to pages 11-12 of the submission of September 27, 2006, and is incorporated herein by reference. Applicants note that the Examiner has previously acknowledged that Applicants have overcome a rejection based on the combined references without Davenport (see the Office Action dated September 17, 2004). Accordingly, in view of the 131 Declaration and arguments provided herein, Applicants request that the rejection be withdrawn.

CONCLUSION

Based on the foregoing remarks, Applicants respectfully request withdrawal of the rejection of claims and allowance of this application. Applicants believe they are entitled to an examination on the merits of their arguments and evidence. In the event that the Examiner finds a procedural hurdle to such an examination, Applicants respectfully request that the Examiner contact the undersigned by telephone so that a supplemental amendment addressing the procedural aspects can be immediately posted in furtherance of an examination on the merits.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Response to Deposit Account No. **50-3732**, Order No. 13784.105005. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732**, Order No. 13784.105005.

Respectfully submitted,
King & Spalding, LLP

Dated: March 27, 2007

By: 

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